Armed Forces College of Medicine

AFCM

Pathology of Pulmonary Tuberculosis

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Describe the aetiology, pathogenesis, morphology and fate of primary **pulmonary** tuberculosis
2. Correlate the underlying immunological mechanisms with the clinical picture of the patient
3. Outline the methods of spread of primary pulmonary tuberculosis.
4. Differentiate between the pathology and course of primary & secondary TB
5. Analyse the pathogenetic mechanisms and course of infection in secondary pulmonary tuberculosis
6. Describe the morphological features (gross and microscopic) of fibro-caseous tuberculosis of lung

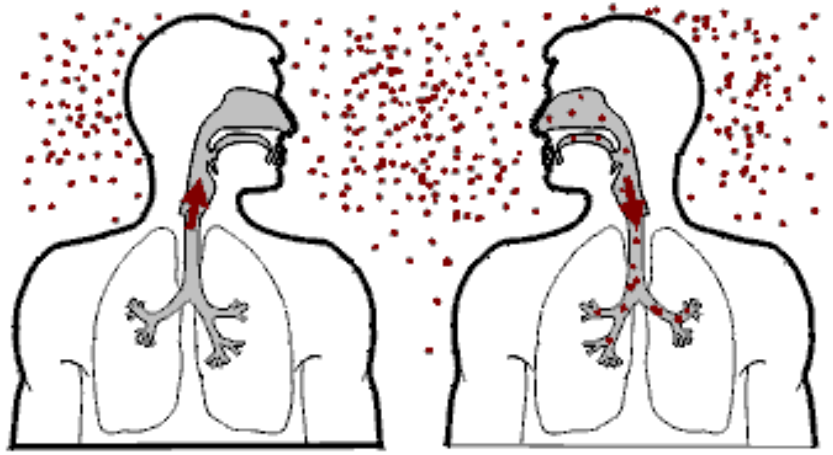
Introduction

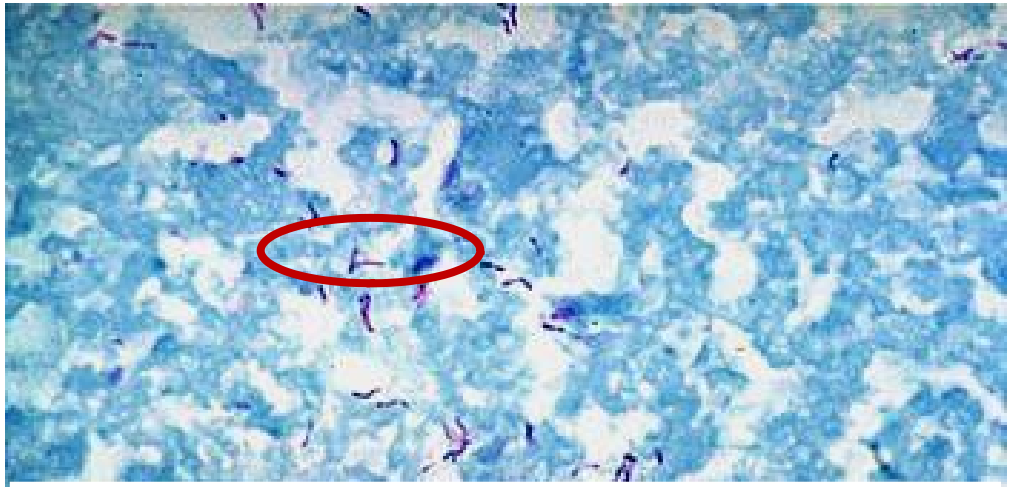
Causes of Granuloma formation

- **Infective granulomas**
  - Bacterial: **Tuberculosis**, Rhinoscleroma and leprosy
  - Spirochetes: syphilis
  - Parasitic: schistosomiasis
  - **Fungal**: histoplasmosis
- **Non infective granulomas**: inorganic metals and dusts (silicosis)
- **Unknown cause : sarcoidosis**

Introduction

- Definition: A chronic inflammatory granulomatous disease caused by **Mycobacterium tuberculosis**
- **Inhalation**: droplet infection of TB bacilli from the sputum expectorated by a patient with open **pul**



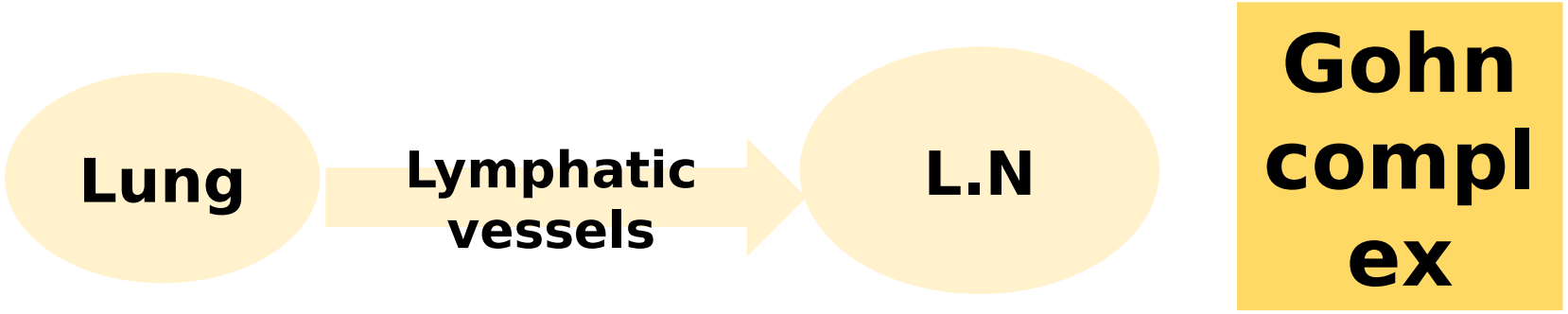


Acid fast bacilli – Zeil Nelson stain

Tuberculosis
Pathology

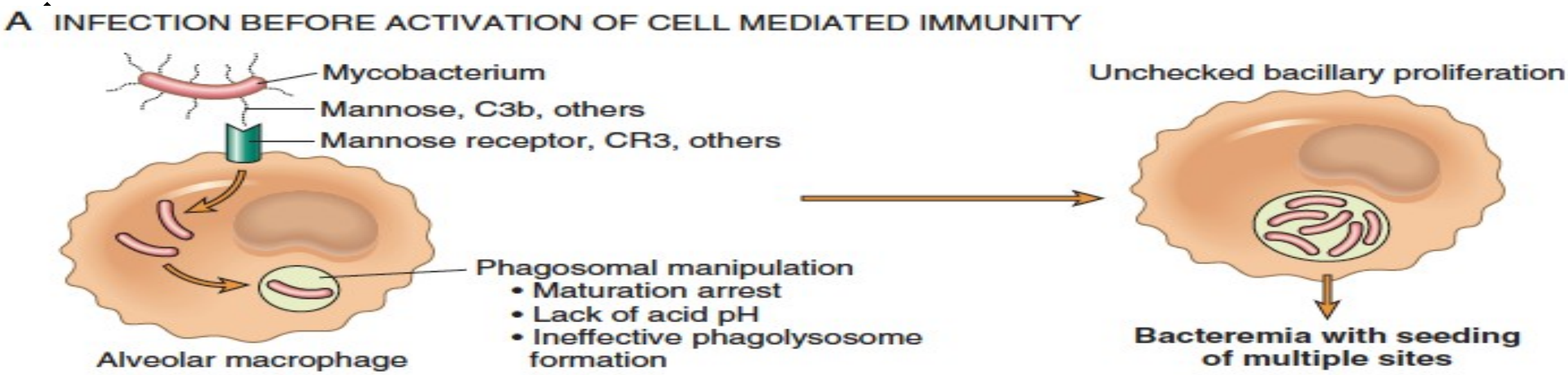
Tubercle bacilli will exist in 3 sites forming tubercles

1- Infected organ: (Primary tuberculous focus)
2- Draining lymphatics: (Tuberculous lymphangitis)
3- Draining lymph nodes: (Tuberculous lymphadenitis)



Primary pulmonary Tuberculosis Pathogenesis

- Develops in a **previously unexposed** (un-sensitized) person.
- Alveolar macrophages are the primary cells infected with M. Tuberculosis
- M. tuberculosis blocks the fusion of the lysosome with the phagosome allowing the bacteria to proliferate “unchecked” within the macrophages



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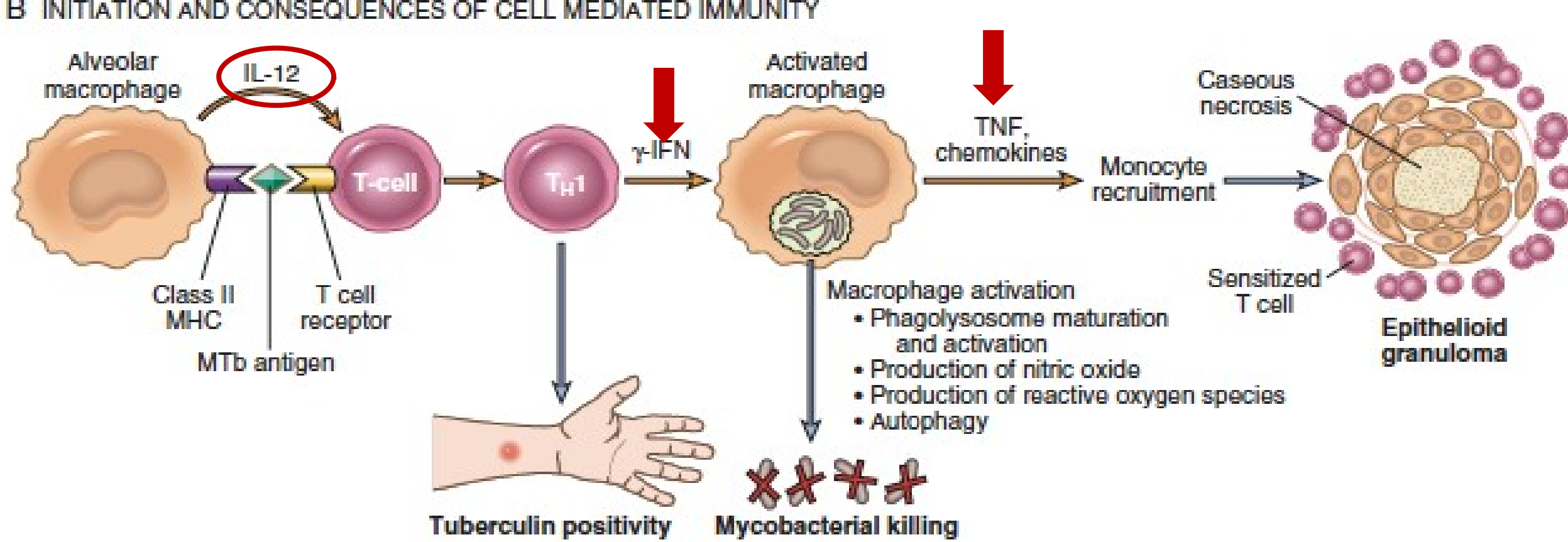
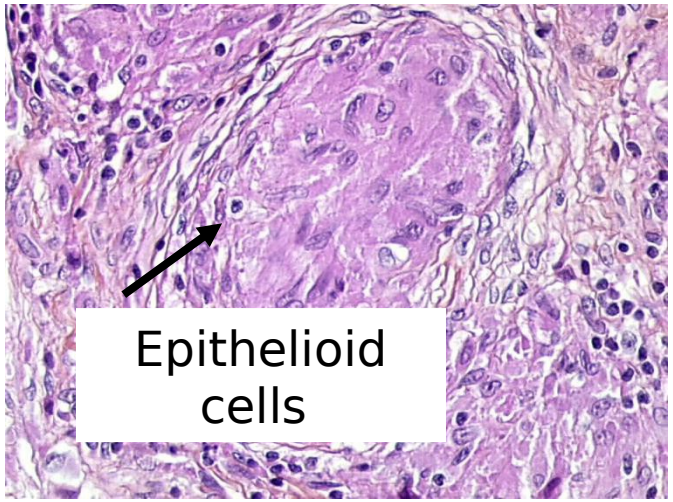
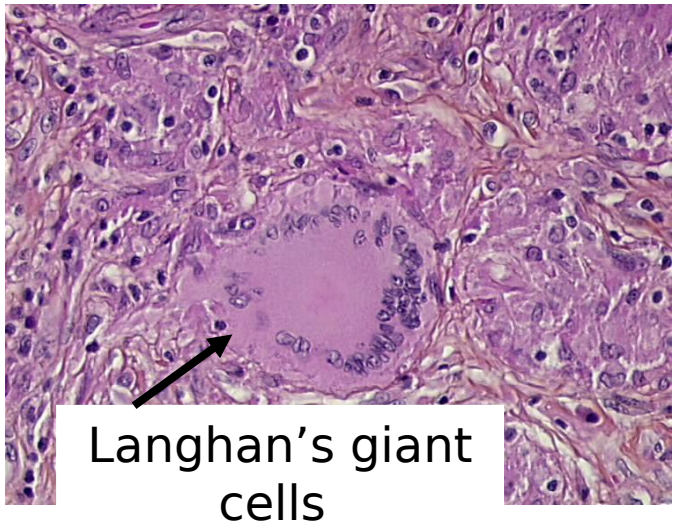
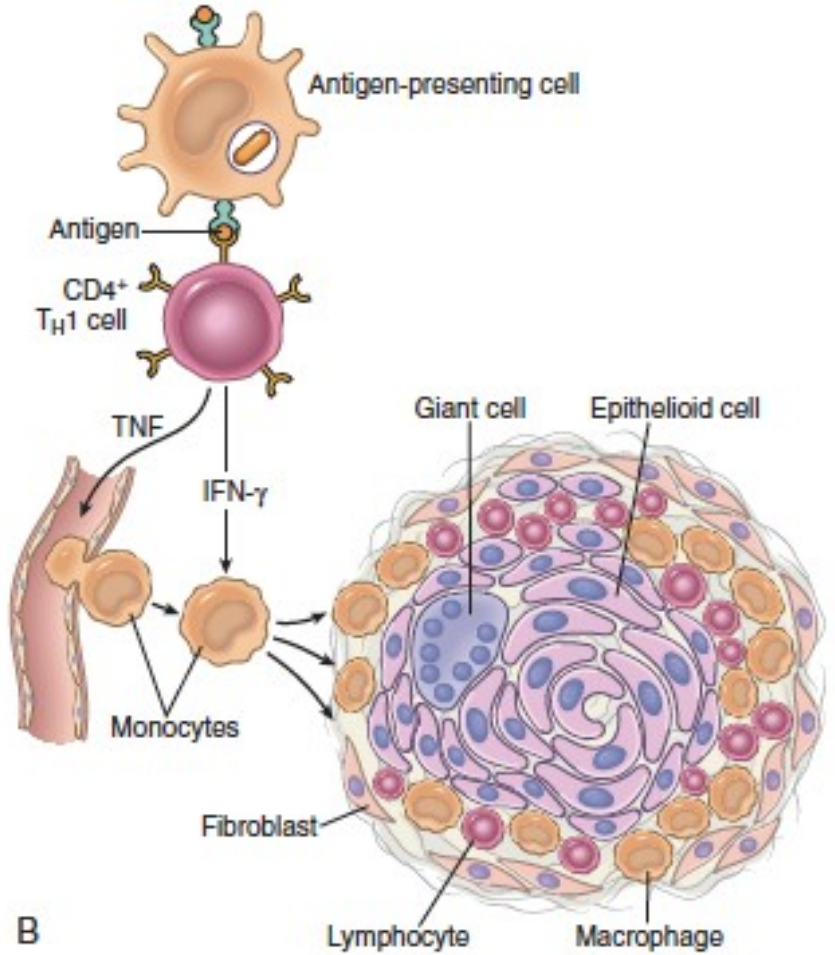


- **In the hilar lymph nodes** , macrophages present the mycobacterial antigens in association with class II MHC molecules to the helper CD4+ T- cells.
- Under the influence of macrophage secreted **IL-12**, $CD4^{+}$-T cells are activated to TH1- cells capable of secreting IFN-gamma (3 weeks)
- **IFN- gamma** activates macrophages into large cells (Epithelioid cells). Activated macrophages secrete **TNF** (to recruit more monocytes) leading to granuloma formation and also produce NO for microbial killing
- Conversion to a **Positive skin Tuberculin test (PPD)** due to hypersensitivity reaction

Primary pulmonary Tuberculosis Morphology







- Activated macrophages that are called "**EPITHELIOID CELLS"**
- Some of these epithelioid cells fuse together forming "**LANGHAN's GIANT CELLS**"

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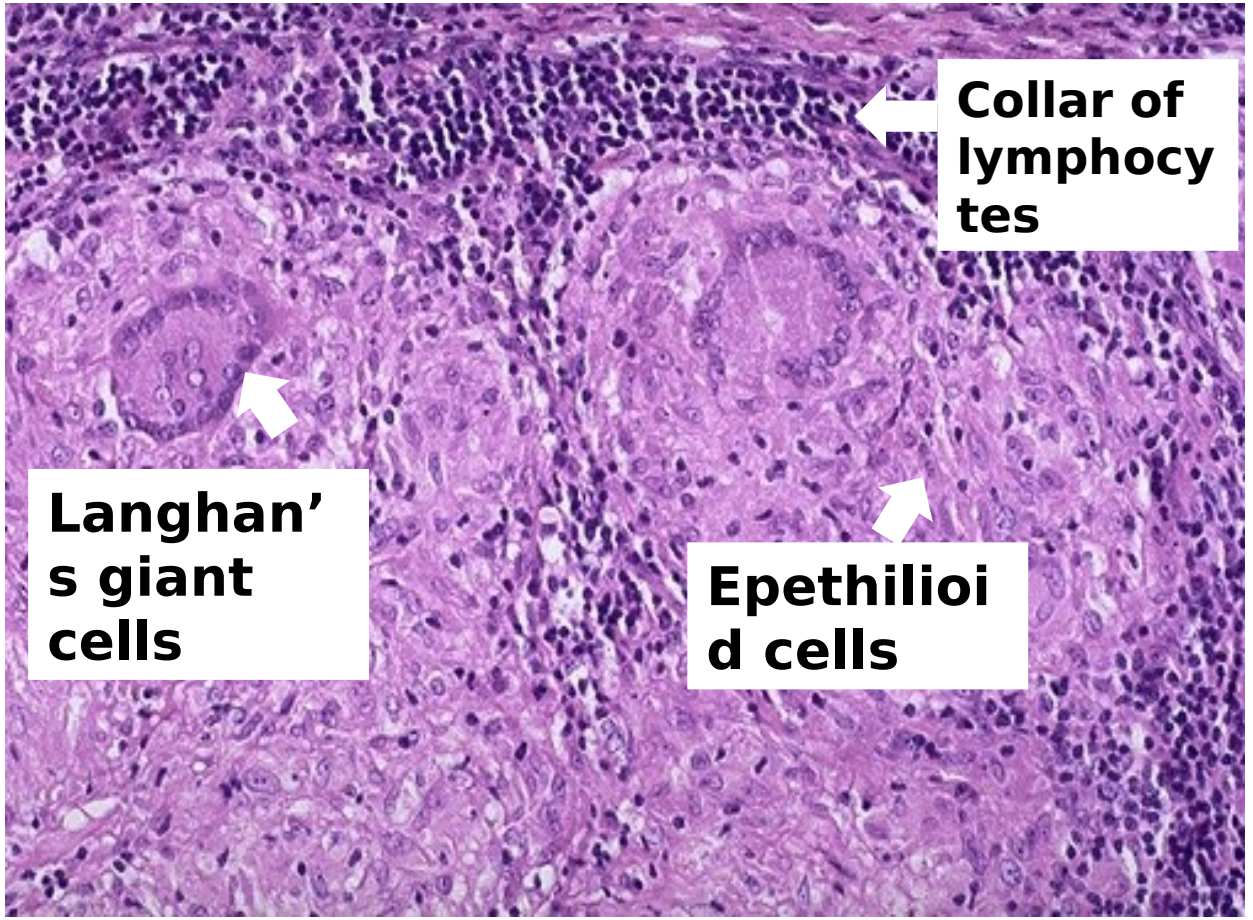
Primary pulmonary Tuberculosis Morphology

- Now the granuloma is called “**TUBERCLE”** and is formed of epithelioid cells, Langhan's giant cells surrounded by a collar of lymphocytes And rimmed at the periphery by some fibrocytes (older granulomas)



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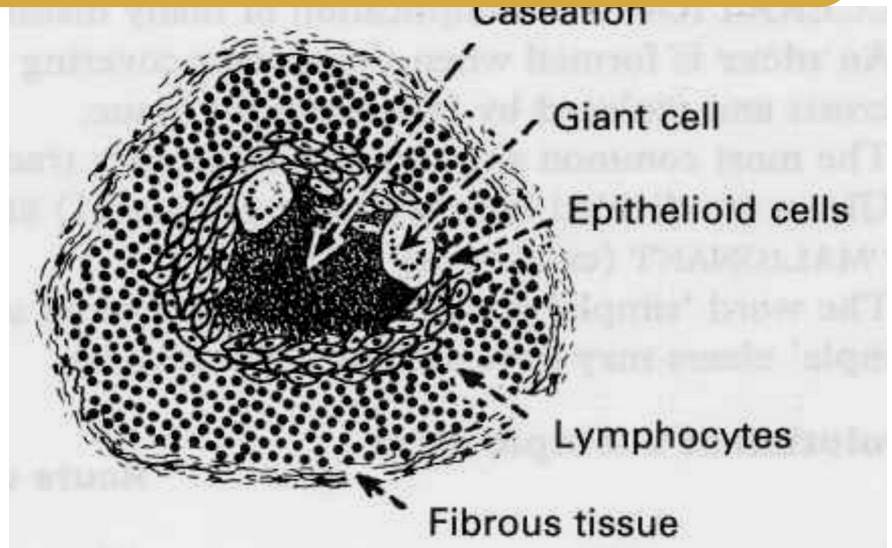
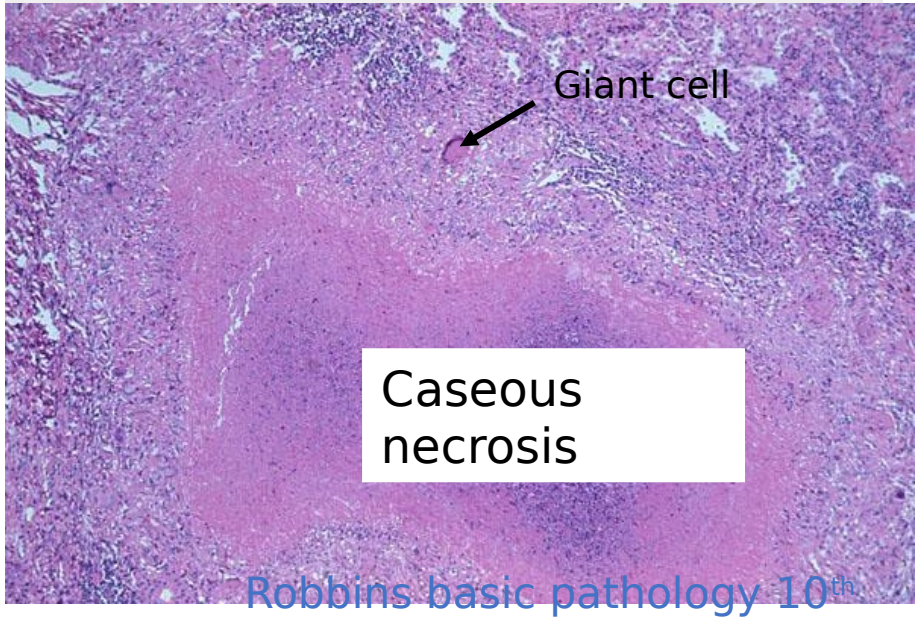
Primary pulmonary Tuberculosis
Morphology

- Later, the center of the tubercle undergoes **caseous necrosis** due to:
  - Avascularity of the lesion
  - Response to mediators released by macrophages and TH-1 cells
- TH-1 cells also stimulate CD8+cytotoxic T- cells to kill macrophages Thus adding to further necrosis and softening





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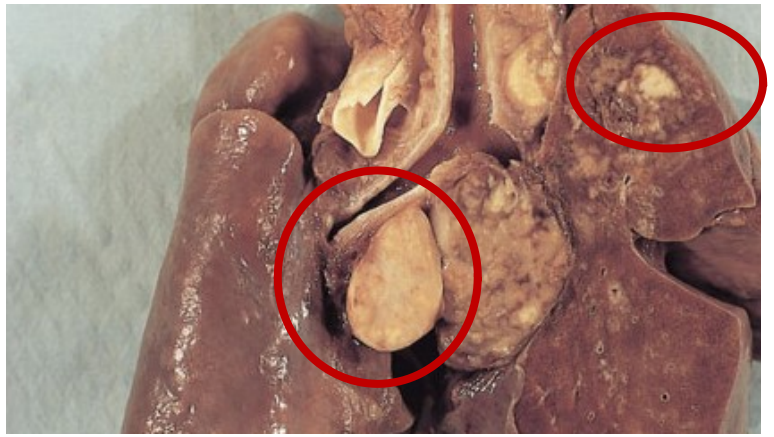
Primary pulmonary Tuberculosis
Morphology



1. Ghon's focus:

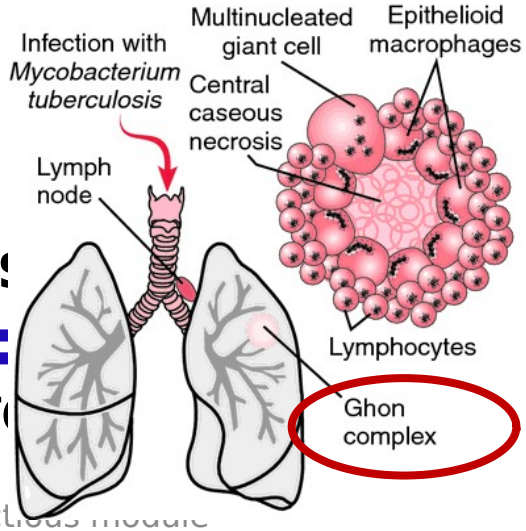
Gross: A subpleural lesion 1-2 cm in diameter-in lower aspect of upper lobe or upper aspect of lower lobe- Later, it becomes yellowish and caseous

Microscopic pic : Adjacent caseating tubercles

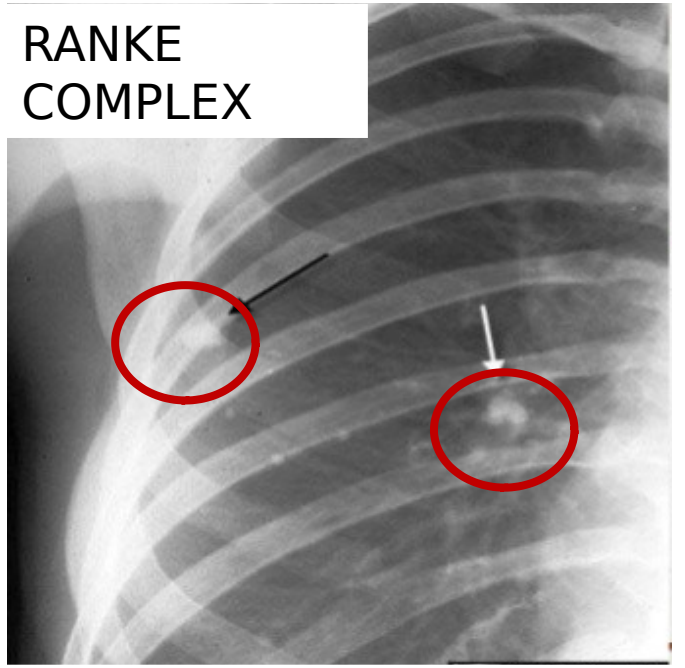
2. lymphangitis: A chain of tubercles along the course of **lymphatic vessel**s

3. Tuberculous lymphadenitis:

- **Early:** enlarged, firm & discr LN
- **Caseation** : soft & yellow



RANKE COMPLEX



https://www.slideshare.net/devlakhera/radiographic-manifestations-of-pulmonary-tuber

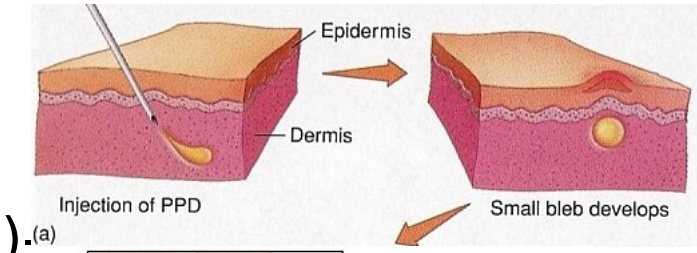
Primary pulmonary Tuberculosis
Fate (outcome)

Outcome is dependent on the adequacy of the host response

1. **Adequate immunity (localization)(90%)**

   The dev. of cell mediated immunity controls the infection and the lesions heal by fibrosis (+/-dystrophic calcification). Appears on x-ray as **RANKE COMPLEX**)

   N.B. Patient is Asymptomatic but has positive PPD (Mantoux test)



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2. **Inadequate immunity (5%)**: leads to **Progressive pulmonary TB** with **SPREAD** of the bacilli (lymphatic- blood- bronchial- brain)

3. In 5% of the cases Some bacilli may remain alive and dormant within the healed lesions, particularly the capsulated ones to become **reactivated** when immunity is

Primary pulmonary Tuberculosis

SPREAD

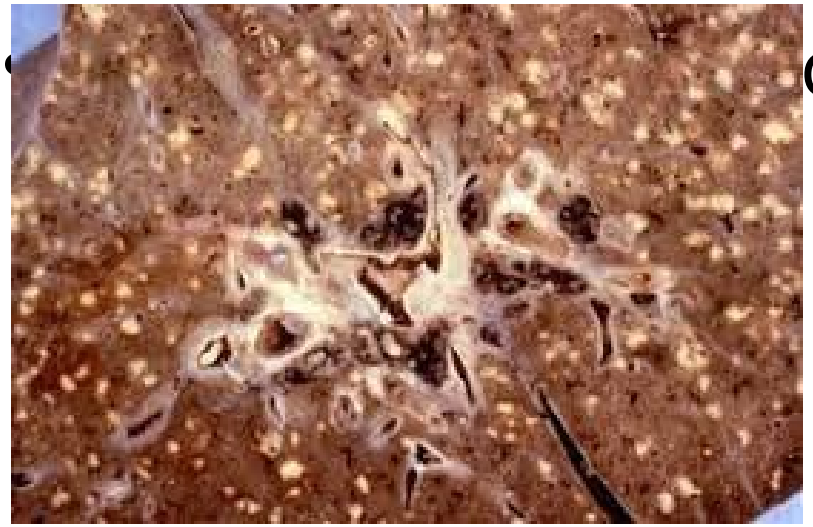
1. **Blood spread** : the result will depend on the number of infecting bacteria
   - **Small** number→ **No effect** (bacteria destroyed by organs' phagocytic cells)
   - **Moderate** number→ **Isolated organ tuberculosis** :one or few organs
   - **Large** number → **Miliary tuberculosis**

2. **Bronchial spread :** caseous erosion of a bronchus from a Ghon's focus or hilar lymph node lead to **Tuberculous bronchopneumonia**

3. **Coughing of infected sputum** lead to tuberculosis of the larynx and tonsils

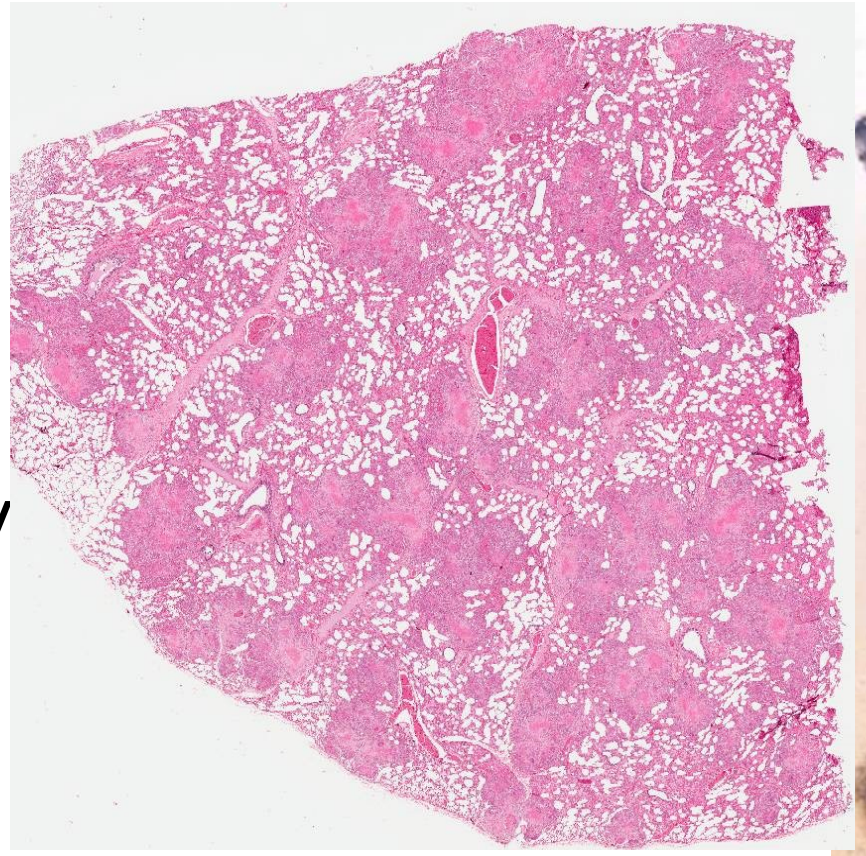
Miliary Tuberculosis

- Large number of tubercles
- Each is 1-2mm in diameter
- [illegible]dly



www.wellcomcollection.org

Miliary TB of the lung



www.blog.nus.edu.sg

Histomicrograph of lung military TB

Miliary TB of the lung

Courtesy of Kasr El Einy pathology museum

Secondary Tuberculosis

- Infection arising in a **previously sensitized host**
- result of **Reactivation** or less commonly **Re-infection**
- lymph node involvement is inconspicuous.
- May follow shortly after primary tuberculosis, but more commonly it arises from reactivation of dormant primary lesions many decades after initial infection (when host resistance is weakened)
- Less than 5% of patients with primary disease develop secondary tu

Secondary tuberculosis common sites

I. **Lung**
II. **Small intestine**
III. **Tonsils**
IV. **Skin**

Primary/secondary Tuberculosis

	Primary T.B infection	Secondary T.B infection
Definition	Exposure for the first time.	Reinfection (Exogenous or endogenous) OR re-activation
Age	More common in children	More common in adults
Sites of lesion	lungs, tonsils, intestine and skin	Anywhere
Parenchymatous focus	Minimal, small	Maximum destruction, large
Cell-mediated immunity	Not present before infection	Well developed
Delayed hypersensitivity	Not present before infection	Well developed
Lymph node involvement	Present (as a part of primary complex)	Absent
Caseation necrosis	Minimal	Extensive
Fate	95% good fate (scarring)	95% bad (spread)

Secondary Pulmonary Tuberculosis
Course of infection

- **Disease severity depends on :**

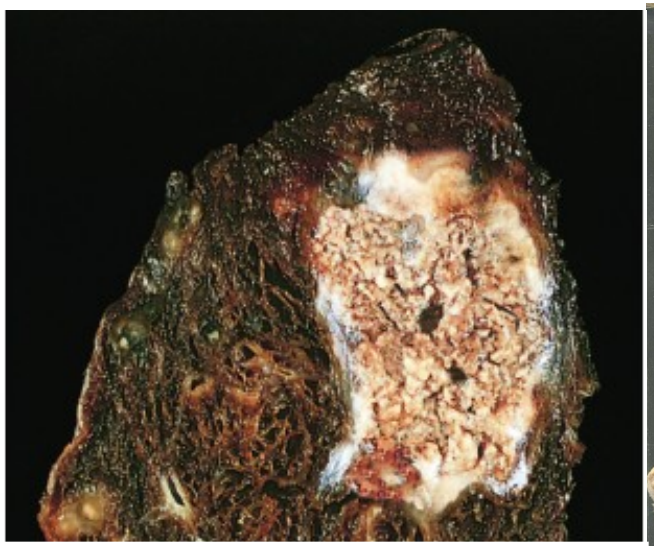
1-Dose & virulence of the bacteria

2- Degree of immunity & hypersensitivity

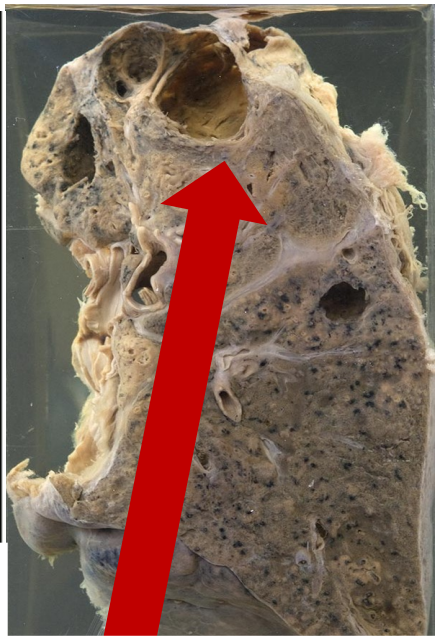
- **The lesions may be:**
  1. **Minimal** and undergo fibrosis leaving a small calcific scar
  2. **Progressive** disease causing "**Chronic fibrocaseous pulmonary tuberculosis**"

Fibrocaseous TB of the lung
Gross picture

- Lesions start in the **APEX** of one or both lungs
- Progressive caseation →bronchial erosion→ evacuation of the caseous material through the eroded bronchus→ formation of a **CAVITY**
- Because of the pre-existing hypersensitivity, the immune response leads to walling off of the focus (no LN involvement)



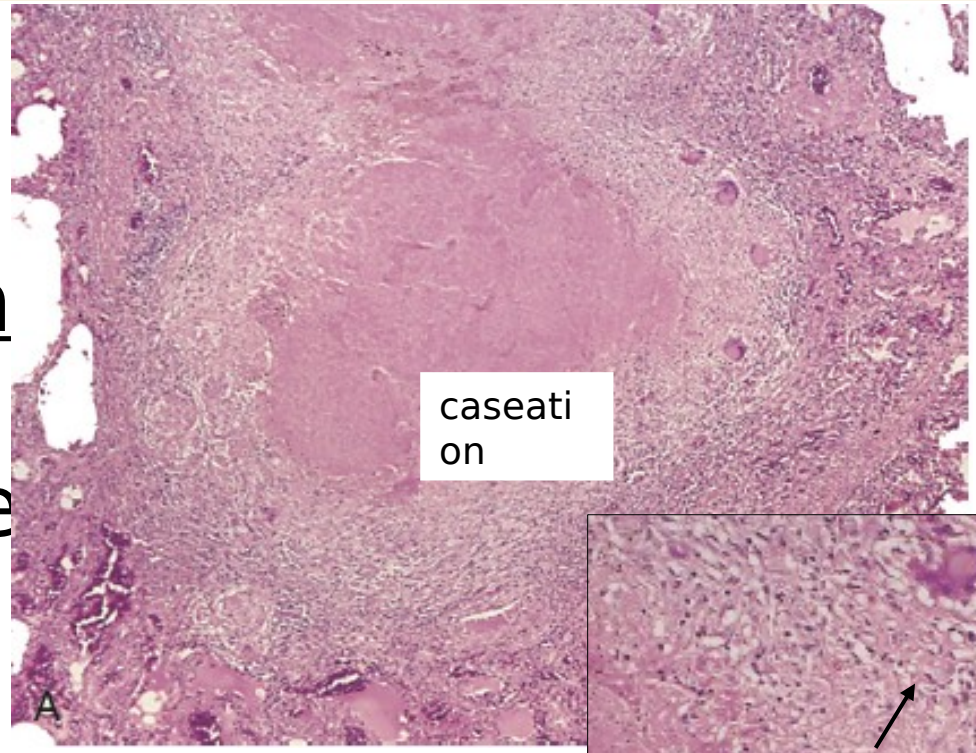
Tuberculosis of the lung with a large area of caseous necrosis containing yello white cheesy material

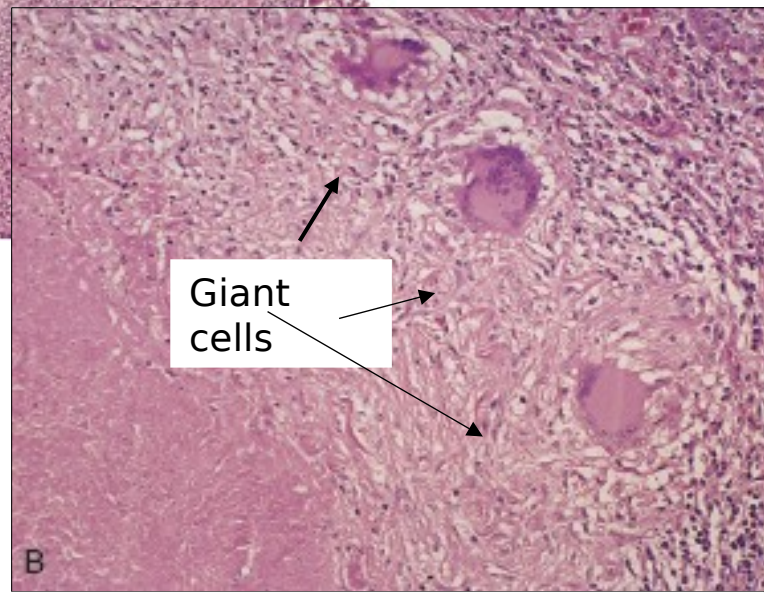


CAVITY: Irregular with caseous lining-Thickened wall due to fibrosis.- Traversed by thick ridges (thick vessels due to end arteritis) that may be destroyed leading to severe

Fibrocaseous TB of the lung
Microscopic picture

- Large areas of **caseation** surrounded by Fibrosis
- Scattered tubercles forme of
  - ❖ Epithelioid cells
  - ❖ Langhan's giant cells
  - ❖ Lymphocytes





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Fibrocaseous TB of the lung
Fate and complications

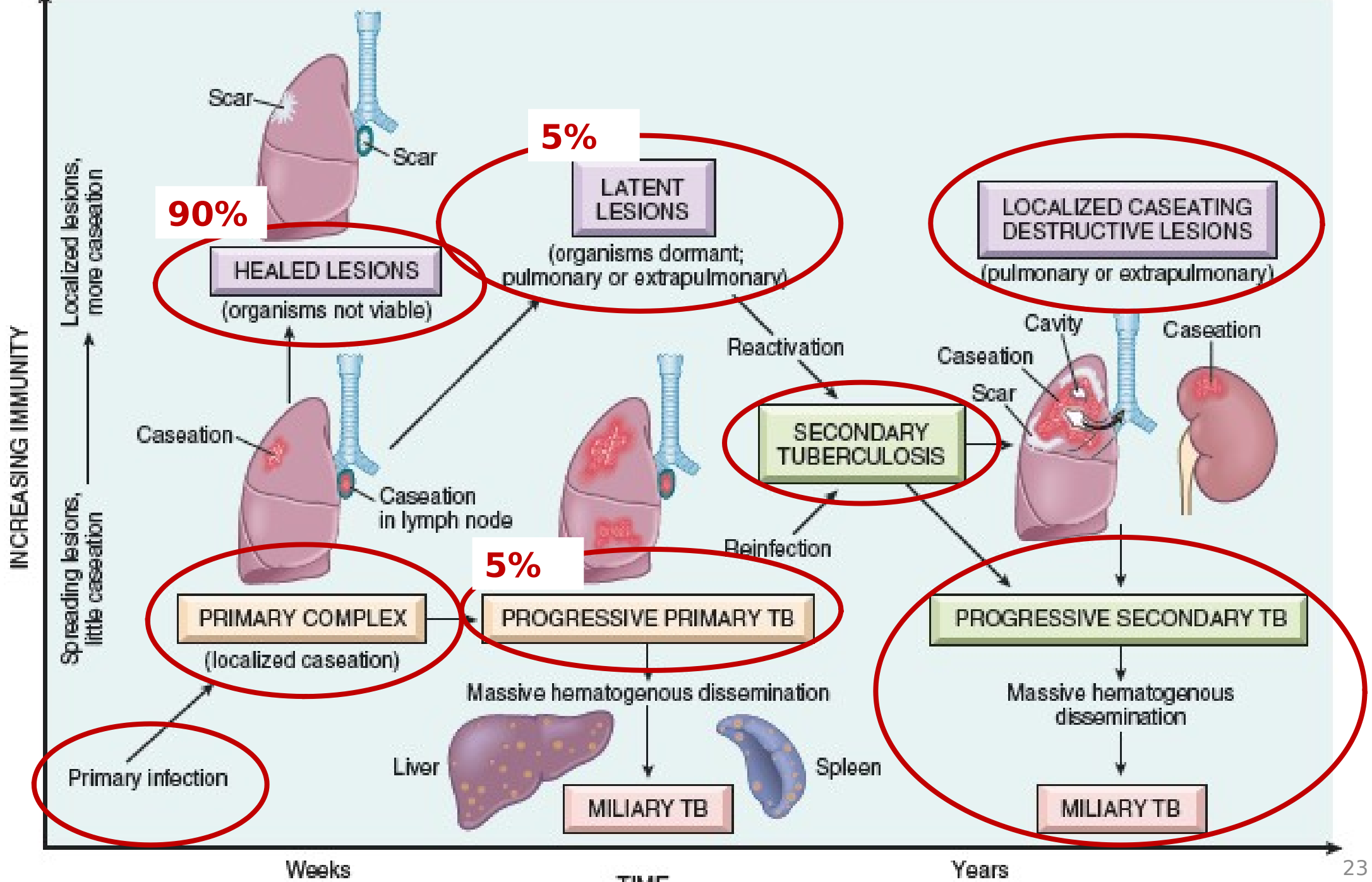
undergoes calcification

2. Large area of caseation erodes nearby bronchus with evacuation and expectoration of the caseous material (progressive pulmonary TB)
3. Erosion of blood vessels traversing the cavity lead to **Hemoptysis**
4. Spread of infection to the lymphatics then back to lung via pulmonary arteries leading to **miliary pulmonary disease**
5. Spread of infection to the pleura; pleural effusions, tuberculous empyema and obliterative fibrous pleurisy
6. Endobronchial and endotracheal spread
7. Hematogenous spread leading to **Systemic military tuberculosis/ isolated organ TB**
8. Rupture of the cavity into the pleural sac leading to **Pneumothorax**
9. **Right sided heart failure** due to bilateral lung fibrosis in bilateral cases

Fibrocaseous TB of the lung
Clinical Picture

- Can be asymptomatic
- Weight loss ,anemia, pallor
- fever (remittent low grade appearing each afternoon and then subsiding) and **night sweats**.
- Cough and expectoration of sputum (containing Tubercle bacilli)
- Hemoptysis
- Pleural effusion, pleuritic chest pain and dyspnea

Always consider pulmonary TB in HIV patients (picture differs according to CD4+ count)


INCREASING IMMUNITY
Localized lesions, more caseation
Spreading lesions, little caseation
Scar
Scar
90%
HEALED LESIONS
(organisms not viable)
5%
LATENT LESIONS
(organisms dormant; pulmonary or extrapulmonary)
LOCALIZED CASEATING DESTRUCTIVE LESIONS
(pulmonary or extrapulmonary)
Reactivation
Cavity
Caseation
Caseation
Scar
Caseation
Caseation in lymph node
SECONDARY TUBERCULOSIS
Reinfection
5%
PRIMARY COMPLEX
(localized caseation)
PROGRESSIVE PRIMARY TB
PROGRESSIVE SECONDARY TB
Massive hematogenous dissemination
Massive hematogenous dissemination
Liver
Spleen
MILIARY TB
MILIARY TB
Primary infection
Weeks
TIME
Years

Quiz

A previously healthy, 20-year-old woman has had a low-grade fever for the past 2 weeks. On physical examination, her temperature is 37.7°C; there are no other remarkable findings. The gross appearance of th lung shown in the figure is representative of her disea Which of the following pathological findings is most lik to be found in this patient?

A. Similar lesions in different organs
B. Similar lesions all over the other lung
C. Ulcers in the small intestine
D. Enlarged hilar lymph nodes
E. Matted intestinal lymph nodes

Quiz-1

A 10-year-old girl who participated in a routine health screening program developed a 10-mm area of induration on the left forearm 3 days after intracutaneous injection of 0.1 mL of purified protein derivative (PPD). She appears healthy. A screening chest radiograph is performed. Which of the following is most likely to be seen on the radiograph?

A. Marked hilar adenopathy
B. Upper lobe calcifications
C. Cavitary change
D. Bilateral pleural effusions
E. No abnormal findings

SUGGESTED TEXTBOOKS

1. Robbins basic pathology; 10th edition, chapter 5 pages; Diseases of the immune system. Pages 142-145
2. Robbins basic pathology; 10th edition, chapter 9 pages; General pathology of infectious disease. Pages 357-359
3. Robbins basic pathology; 10th edition, chapter 13 pages; Lung pages 526-528
4. https://www.khanacademy.org/science/health-and-medicine/infectious-diseases/tuberculosis/v/tb-pathogenesis